

What is claimed is:

1. A double-stranded RNA complex comprising:
 - (c) a first ribonucleic acid molecule capable of hybridizing under physiological conditions to at least a portion of an mRNA molecule; and
 - (d) a second ribonucleic acid molecule wherein at least a portion of the second ribonucleic acid molecule is capable of hybridizing under physiological conditions to the first portion.
2. A RNA complex of claim 1 wherein the first and second portions are separate ribonucleic acid molecules.
3. A double-stranded RNA molecule of claim 1 wherein the mRNA is encoded by a gene in a cell.
4. A linear RNA molecule capable of forming a dsRNA complex wherein the RNA molecule comprises:
 - (c) a first portion that hybridizes to at least a portion of a mRNA molecule; and
 - (d) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion to form a hairpin dsRNA complex.
5. A double-stranded RNA molecule of claim 4 wherein the mRNA is encoded by a gene in a cell.
6. A linear RNA molecule of claim 4 further comprising a third portion of ribonucleic acid interposed between the first and second portions.
7. A linear RNA molecule of claim 6 wherein the third portion promotes hybridization between the first and second portion.
8. A RNA molecule of claims 1 or 4 further comprising an additional RNA portion of ribonucleic acid that enhances the ability of dsRNA to alter transcription from the gene encoding the mRNA molecule.
9. A RNA molecule of claim 8 wherein the additional RNA portion encodes an RNA molecule.
10. A RNA molecule of claim 8 wherein the additional RNA portion encodes a protein.
11. A RNA of claim 10 wherein the protein is Tat.
12. A RNA of claim 6 wherein the third portion of ribonucleic acid further comprises at least one ribozyme and a target sequence recognizable by the ribozyme wherein the target sequence is not present in the first portion and the second portion.

13. A RNA of claim 12 wherein the double-stranded RNA complex is formed upon hybridization of the first and second portion and the target sequence is cleaved by the hairpin dsRNA.
- 5 14. A RNA of claim 6 wherein the third portion of ribonucleic acid further comprises an intron or a linker sequence.
15. A linear RNA molecule capable of forming a dsRNA complex wherein the RNA molecule comprises:
- 10 (d) a first portion that comprises a region of RNA that is complementary to at least a portion of a mRNA molecule encoded by a gene;
- (e) a second portion capable of hybridizing to at least part of the first portion; and
- 15 (f) a third portion positioned between the first and second portions to permit the first and second portions to hybridize with one another.
16. A linear RNA molecule of claim 15 wherein the third portion comprises at least one ribozyme and a target sequence recognized by the ribozyme wherein the target sequence is not present in the first or second portion.
- 20 17. A linear RNA molecule of claim 15 wherein second sequence comprises a polyadenylation signal.
- 25 18. A linear RNA molecule of claim 15 wherein the third portion comprises a plurality of ribozymes and target sequences capable of cleavage thereby.
19. A linear RNA molecule capable of forming a dsRNA complex wherein the RNA molecule comprises:
- 30 (c) a first portion that hybridizes to at least a portion of a mRNA molecule encoded by a gene; and
- (d) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion and wherein the second portion comprises a polyadenylation signal and a ribozyme positioned between the part of the second portion capable of hybridizing to the first portion and the polyadenylation signal
- 35 wherein the ribozyme is capable of removing the polyadenylation signal.
- 40 20. A linear RNA molecule of claim 19 wherein the ribozyme is a cis-acting hammerhead ribozyme.
21. At least one DNA molecule encoding the RNA molecules of any of claims 1 – 20.
- 45 22. A DNA molecule of claim 21 wherein a single DNA molecule encodes the RNA molecules of any one of claims 1-20.
23. A DNA molecule of claim 21 wherein two DNA molecules encode the RNA molecules of claim 1.

24. A eukaryotic cell comprising the RNA molecules of claims 1-20.
25. A eukaryotic cell comprising the DNA of molecules of any of claims 21-23.
- 5 26. A eukaryotic cell of claims 24 or 25 wherein the cell is a mammalian cell.
27. A eukaryotic cell of any of claims 24-26 wherein the cell is a human cell.
- 10 28. A cell of claim 27 wherein the cell further comprises HIV nucleic acid.
29. A cell of any of claims 24-27 wherein the cell is a neoplastic cell.
30. A vector encoding at least one of the RNA molecules of any of claims 1-20.
- 15 31. A vector comprising the DNA of any of claims 21-23.
32. A vector of claim 30 or 31 wherein the vector is a plasmid, an adenovirus, an
adenoassociated virus, or a retrovirus.
- 20 33. A vector of claim 32 wherein the plasmid is an episomal plasmid.
34. A method for inhibiting protein expression in a eukaryotic cell comprising the step of
introducing the RNA of any of claims 1-20, the DNA molecules of claims 21-23 or
25 the vectors of claims 30-32 into the cell.
35. A method of claim 34 wherein the eukaryotic cell is a mammalian cell.
36. A method of claim 35 wherein the cell is a human cell, a somatic cell, an
30 undifferentiated, dedifferentiated, neoplastic cell or a chimeric cell.
37. A method of claim 34 wherein the RNA, DNA is introduced into the cell using a
vesicle or is delivered by microinjection.
- 35 38. A method of claim 34 wherein the mRNA is selected from the group consisting of a
cancer-related gene, a rheumatoid arthritis-related gene and a viral gene.
39. A method of claim 38 wherein the mRNA is an HIV-derived gene.
- 40 40. A method of claim 39 wherein the gene is selected from the group consisting of *tat*,
nef, *rev*, *ma*, *ca*, *nc*, *pg*, *vpu*, *pr*, *vif*, *su*, *tm*, *vpr*, *rt* and *in*.
41. A method of inhibiting protein expression from a gene in a cell comprising the step
of;
45 introducing a linear RNA molecule capable of forming a dsRNA complex into a
cell, wherein the RNA molecule comprises:

- (a) a first portion that hybridizes to at least part of a mRNA molecule encoded by a gene; and
- (b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion

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42. A method of claim 41 wherein the second portion comprises a polyadenylation signal positioned at the 3' end of the linear RNA molecule.

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43. A method of claim 42 wherein the second portion further comprises a ribozyme positioned between the part of the second portion capable of hybridizing to the first portion and the polyadenylation signal, wherein the ribozyme is capable of removing the polyadenylation signal.

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44. A method of claim 43 wherein the ribozyme is a *cis*-acting hammerhead ribozyme.

45. A method of claim 41 wherein the cell is a mammalian cell.

46. A method of claim 41 wherein the cell is *in vitro*.

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47. A method of claim 41 wherein the cell is *in vivo*.

48. A method of claim 41 wherein the introducing step employs microinjection.

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49. A method of claim 41 wherein the RNA is encoded by a DNA molecule and the DNA molecule is transcribed in the cell.

50. A method of claim 41 wherein the RNA is introduced as a vector.

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51. A method of claim 50 wherein the vector is RNA or DNA.

52. A method of claim 51 wherein the vector is a plasmid, adenovirus, adeno-associated virus or a retrovirus.

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53. A method of claim 41 wherein the RNA is synthesized outside the cell.

54. A method of claim 41 wherein the RNA is synthesized inside the cell.

55. A method of claim 43 wherein the RNA is retained in the nucleus.

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56. A method for localizing a dsRNA molecule to the nucleus of a cell comprising the step of:

introducing a DNA molecule encoding a linear RNA molecule capable of forming a dsRNA complex into a cell wherein the RNA molecule encoded by the DNA molecule comprises:

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- (a) a first portion that hybridizes to at least a portion of a mRNA molecule encoded by a gene; and
- (b) a second portion wherein at least part of the second portion is capable of hybridizing to the first portion and wherein the second portion comprises a

polyadenylation signal and a ribozyme positioned between the part of the second portion capable of hybridizing to the first portion and the polyadenylation signal,
 wherein the ribozyme is capable of removing the polyadenylation signal thereby retaining the RNA in the nucleus.

57. The method of claim 56 wherein the ribozyme is a *cis*-acting hammerhead ribozyme.

58. A method for modulating expression of a nucleic acid sequence in a cell comprising exposing the cell to culture medium in which cells comprising a dsRNA complex comprising a first portion that hybridizes to at least part of a mRNA molecule encoded by a gene; and a second portion wherein at least part of the second portion is capable of hybridizing to the first portion have been maintained in cell culture.

59. A method of identifying the function of a gene in a cell comprising the step of;

- (a) binding a dsRNA molecule to an mRNA molecule in a cell wherein the dsRNA molecule comprises a first ribonucleic acid molecule capable of hybridizing under physiological conditions to at least a portion of an mRNA molecule; and a second ribonucleic acid molecule wherein at least a portion of the second ribonucleic acid molecule is capable of hybridizing under physiological conditions to the first portion; and
- (b) detecting a change in the cell resulting from the binding.

60. A method of forming a double-stranded RNA in a cell comprising the step of introducing the RNA molecule of any of claims 1-20 or the DNA molecule of claims 21-23 into a cell.

61. A composition for inhibiting the expression of a gene in a eukaryotic cell comprising:

a RNA molecule of claims 1 or 4 wherein the RNA molecule further comprises an additional RNA portion of ribonucleic acid that enhances the ability of dsRNA to alter transcription from the gene encoding the mRNA molecule.

61. The composition of claim 61 further comprising a third portion of ribonucleic acid interposed between the first and second portions wherein the third portion promotes hybridization between the first and second portion.

62. Use of any of the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33 to inhibit expression of a gene in a cell.

63. A pharmaceutical composition comprising the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33.

64. A microinjection apparatus comprising a pharmaceutical composition comprising the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33.

66. A lipid vesicle comprising the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33.
67. Use of any of the RNA of claims 1-20, the DNA of claims 21-23 or the vectors of claims 31-33 to determine the function of genomic nucleic acid or viral nucleic acid in a cell.